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10/041,633	01/10/2002	Akio Kobayashi	111632	6574
25944	7590	01/12/2004	EXAMINER	
OLIFF & BERRIDGE, PLC P.O. BOX 19928 ALEXANDRIA, VA 22320			BERTOGLIO, VALARIE E	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/041,633

Applicant(s)

KOBAYASHI ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/05/2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☒ Claim(s) 7, 9, 10 and 15 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☒ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1, 2, 3 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of the species nucleus in the response to the election of species requirement received 11/05/2003 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search and examine the full scope of the claims. This argument is not persuasive. This is not found persuasive because the claims broadly encompass introducing a huge genera of foreign matter into a cell, including organelles such as nuclei, chloroplasts and mitochondria, nucleic acids including DNA, RNA, antisense, plasmids, and chromosomes, proteins, or other compounds including organic and inorganic compounds. It is maintained that it would be an undue burden to search and examine each species of foreign matter. Applicant also notes that claims 1-9 and 11-15 read on the elected species. Claims 1-7 and 11-14 do not include the step of introducing foreign matter into a cell and therefore does not read on the elected species.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15 with respect to the elected specie, nucleus, are pending and under consideration in the instant office action.

### ***Claim Objections***

Claim 7 objected to because of the following informalities: Claim 7 appears to contain a typographical error as it reads "nitrogen-exited" rather than "nitrogen-excited" in line 3. Appropriate correction is required.

Claims 9,10 and 15 are objected to as being drawn to non-elected subject matter.

### ***Claim Rejections - 35 USC § 112-1<sup>st</sup> paragraph***

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for processing a cell comprising irradiating a cell with a laser beam through an optical fiber and removing or boring a hole in a cell wall, does not reasonably provide enablement for irradiating a cell with a laser beam through an optical fiber and removing or boring a hole in a cell membrane or an entirety of the cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are directed to a method for processing a cell comprising irradiating a cell or living tissue with a laser beam through an optical fiber and cutting of, removing or boring a cell wall and/or cell membrane or an entirety of the cell. Dependent claims add limitations that the wavelength of the laser beam be 500nm or less (claim 2), that the cell is irradiated with the laser through reflection and condensing (claims 3-6), and that the laser be either a YAG, excimer, Ar, nitrogen, or nitrogen excited laser (claim 7). Claims 8-10 require an additional step of introducing material into the cell through a laser irradiated portion of a cell. Claims 11-14 depend from claim 1 and add additional limitations to the fiber optic fiberguide including that the fiberguide be hollow (claim 11), be filled with inert gas (claims 12 and 13) and be coated with metal (claim 14). Claim 15 is directed to a transformed body.

The specification teaches using a quartz fiber optic fiberguide to deliver a laser to the cell wall of a plant cell. The specification teaches transmitting a 193 nm ArF excimer laser beam

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through a quartz fiber (page 10, paragraph 0043) and a quartz capillary coated with aluminum (page 9, paragraph 0042 and page 10, paragraph 0044). An onion skin epidermic cell was irradiated with the laser, removing the cell wall (page 10, paragraph 0046). The cell was still alive after 24 hours.

The specification also teaches introducing a laser into a hollow quartz fiber wherein the hollow space is filled with nitrogen, which increases laser intensity (page 11, paragraph 0047). The hollow fiber allowed for flexibility of the laser (page 11, line 6). The specification teaches attaching an aluminum deposited quartz glass chip to the optical fiber to condense the laser (page 12, paragraph 0051). The laser was used to bore a 2  $\mu$ m hole in the cell wall of an onion epidermic cell (page 12, lines 18-19). Plasmid encoding GFP was injected through the hole into the plant cell and GFP fluorescence was assessed, however, the specification does not teach that fluorescence actually occurred (page 13, paragraph 0053).

1) The breadth of the claims encompasses boring a cell wall or a cell membrane of a plant or animal cell. The nature of the invention involves boring a hole into a cell for the purpose of allowing introduction of genetic material into the cell. The utility of boring a hole through a plant cell wall is to facilitate the introduction of genetic material by avoiding protoplast preparation for plant cells because injection through the cell wall is problematic and extremely difficult (page 2, paragraph 0004).

The specification does not enable boring a hole in a cell membrane wherein the hole is large enough for a nucleus to be introduced. The specification teaches removing a cell wall from a plant cell and also teaches boring a plant cell wall resulting in a 2 $\mu$ m hole. The specification teaches injecting DNA into the cell through the small, bored hole of the cell wall and puncturing

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through the intact cell membrane (page 13, paragraph 0052). The specification fails to provide the guidance necessary for one of skill in the art to bore through a cell membrane, creating a hole large enough to accommodate a nucleus. The art at the time of filing taught using lasers to ablate or kill cells. Chamberlin (1993, Development, Vol. 118, pages 297-324) taught using a laser to selectively ablate cells to determine how cellular signals effect cell fate specification. Kuang (2001, J. Neurobiol., Vol. 47, pages 1-15) taught using a laser to specifically ablate the ENC1 cell to test the role of ENC1 in embryonic rotation. With respect to the size of the hole required for introduction of a nucleus in a cell, EP0483847A2 (1991) taught that holes bored into the cell envelope (including the cell wall and cell membrane) must be no more than 5 to 500 nm. Weber (1988, Plant Cell, Tissue and Organ Culture, Vol. 12, pages 219-22) taught using a laser to introduce a small hole, large enough for DNA to diffuse through using a laser with a diameter of 100 nm. The laser used in the instant specification is much larger, in the range of 0.5 to 100  $\mu\text{m}$  (page 7, paragraph 0029). The specification does not provide the guidance necessary for one of skill in the art use a laser on a cell to selectively introduce a pore large enough to accommodate a plant or animal cell nucleus and not kill or harm the cell. Moreover, the specification does not provide guidance correlating to non-lethal manipulation of a cell other than manipulation of the cell wall. It would require undue experimentation for one of skill in the art at the time the invention was made to determine how to bore a hole in a cell membrane large enough to accommodate a nucleus, using a laser beam.

2) The breadth of the claims 8-10 encompasses introducing a nucleus into a cell or into a cell wherein the entirety of the cell has been removed or bored by laser irradiation. The specification does not enable introducing a nucleus into a cell that has been irradiated in such a

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manner as to remove or bore the entire cell. Such a cell would be ablated and unfit for introducing a nucleus. The specification has not provided guidance that correlates irradiation of a cell in its entirety, wherein said cell remains viable to allow for the introduction of a nucleus. If some structure of the cell remained after laser ablation, said structure would be dead. One could introduce a nucleus into said dead cell, however, the specification does not teach how one of skill in the art would use a dead cell comprising an exogenously introduced nucleus.

The claims also read on a transgenic plant produced by introducing a transgenic nucleus into a plant cell. The specification teaches introducing a DNA into a plant cell, leading to expression of the transgene. However, the specification provides no correlation to generating a transgenic plant by introducing a nucleus. The claims further encompass somatic cell nuclear transfer (animal cloning). The art at the time of filing taught that this technology was highly underdeveloped and the effects of somatic cell nuclear transfer on an animal generated therefrom are not predictable, controllable or understood (refer to Denning, 2001, *Nature Biotechnology*, Vol. 19, pages 559-562; Dinnyes, 2002, *Cloning and Stem Cells*, Vol. 4, pages 81-90; McCreath, 2000, *Nature*, Vol. 405, pages 1066-1069; Kent-First, 2000, *Nature Biotechnology*, Vol. 18, pages 928-929). Therefore, it would require one of skill in the art undue experimentation to determine how to introduce a nucleus into a cell or into a cell wherein the entirety of the cell has been irradiated with a laser and how to use said cell.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction and/or guidance provided by the specification, and the breadth of the claims with respect to boring a cell membrane to accommodate a nucleus and

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to boring the entirety of a cell, it would have required undue experimentation for one skilled in the art to make and use the claimed invention without a reasonable expectation of success.

***Claim Rejections - 35 USC § 112-2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear as it contains the terminology "and/or". It is not clear whether claim 1 is referring to boring through a cell wall and a cell membrane simultaneously, or to boring through only a cell wall or to boring through a cell membrane, leaving the cell wall intact.

Claims 2-15 depend from claim 1.

Claim 6 is unclear because it contains an improper Markush group. The claim contains the term "and/or" in the Markush group. The term "or" in a Markush group is unclear because it is not clear that the "group" does or does not consist of the listed limitations. Furthermore, it is unclear if the claim is referring to oxides of all of the metals listed in the claim or to oxides of just some of the listed metals.

Claim 15 is unclear because it refers to a transformed body. It is not clear if the transformed body is referring to a cell or a body of an organism. The term transformed is also



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unclear as it is not clear whether it is referring to genetic transformation or oncogenic transformation.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Silkiss (1993, Ophthalmic Surgery, Vol. 24, pages 772-774).

Claim 1 is drawn to a method of processing a cell comprising irradiating a cell with a laser beam through an optical fiber and removing or boring an entirety of the cell thus irradiated. Claim 7 limits the laser to a YAG laser, an excimer laser, an Ar ion laser a, nitrogen excited laser, or a nitrogen laser.

Silkiss taught passing a quartz fiber optic (page 772, col. 2, lines 19-21) through the superior punctum and canalicular system to the lacrimal sac where laser energy was used to ablate cells of the nasolacrimal duct lining (Abstract, page 772, col.2, lines 37-39). Silkiss taught that the laser was a YAG laser (page 772, col. 1, line12).

Thus, Silkiss meets the limitations of claims 1 and 7.

2) Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Henriksen (1997, Eur J Physiol., Vol. 433, pages 832-841;IDS).

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Claims are drawn to a method for processing a cell comprising irradiating a cell or living tissue with a laser beam through an optical fiber. Claim 2 introduces the limitation that the wavelength of the laser be 500 nm or less. Claim 3 adds the limitation that the laser is reflected and condensed. Claim 7 adds the limitation that the laser is a YAG laser, an excimer laser, an Ar ion laser, a nitrogen laser or a nitrogen-excited laser.

Henriksen taught using a nitrogen laser with a wavelength of 337.1 nm (page 833, col. 1, 2<sup>nd</sup> to last para.; col. 2, line 16) that is reflected and condensed (paragraph bridging pages 834-835) to ablate a portion of a plant cell wall (page 838, col. 2, para. 2), giving access to the protoplast for a patch clamp .

Thus, Henriksen meets the limitations of claims 1-3 and 7.

3) Claims 1, 2 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Abela (USPN 5,586,982, IDS).

Claims are drawn to a method for processing a cell comprising irradiating a cell or living tissue with a laser beam through an optical fiber. Claim 2 introduces the limitation that the wavelength of the laser be 500 nm or less. Claim 7 adds the limitation that the laser is a YAG laser, an excimer laser, an Ar ion laser, a nitrogen laser or a nitrogen-excited laser.

Abela teaches applying laser energy consisting of a 355 nm YAG laser (column 7, lines 40-42) transmitted through a fiber optic bundle (col. 5, lines 45-46; Figure 2; Figure 17) to porate cells (column 4, lines 54-56) followed by introducing a genetic material following laser treatment (column 8, lines 19-22).

Therefore, Abela satisfies all of the limitations of claims 1, 2 and 7.

4) Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Kwon (1997, Oncogene, Vol. 15, pages 2625-2631).

Claim 15 is drawn to a transformed body, which, in light of the specification, is interpreted as being a transformed cell (see the rejection of claim 15 under 35 U.S.C. 112, 2<sup>nd</sup> paragraph, above). It is accepted in the art that a transformed cell can refer to a cell that has undergone oncogenic transformation. Therefore, claim 15 is interpreted as encompassing a cell that has undergone oncogenic transformation.

Claim 15 is a product by process claim in which the process of creating the transformed body carries little patentable weight. It is only the product, which is anticipated by the prior art and not the process by which the product was made. This is because the final product (a transformed body) is not distinguished by any particular features or characteristics resulting from the process by which it is made. As such, the limitations of the claimed transformed body are met by any transformed body in the prior art. Patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985).

Kwon teaches fibroblasts transformed with oncogenic agents (page 2626, col. 1, lines 3-5) as well as spontaneously transformed cells such as HeLa cells (page 2626, col. 2, line 5).

Therefore, Kwon satisfies all of the limitations of claim 15.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abela (USPN 5,586,982, IDS) taken with Brauer (USPN 5,951,543 filed 06/30/1997) and Harrington (USPN 5,951,543, filed 06/30/1997).

Claim 1 is drawn to a method for processing a cell comprising irradiating a cell or living tissue with a laser beam through an optical fiber. Claim 11 adds the limitation that the quartz fiber is hollow.

Abela taught applying laser energy to a cell (column 4, lines 54-56) transmitted through a fiber optic waveguide (col 5, lines 45-46; Figure 2; Figure 17). Abela did not teach that the quartz fiber used was hollow.

However, at the time the claimed invention was made, Brauer taught using a flexible, hollow waveguide (Abstract, line 2; col. 4, lines 40-48) to introduce a laser in vivo because the hollow waveguide offers greater flexibility for in vivo manipulation (Abstract; col. 5, line 11; col. 7, lines 1-6). Harrington taught making a flexible hollow waveguide for transmitting laser radiation with low attenuation (abstract; col. 1, lines 29-32 and 47-51).

Accordingly, it would have been obvious at the time the claimed invention was made, to use the laser of Abela using the hollow fiber optic waveguide of Brauer. One of ordinary skill in the art would have been sufficiently motivated to replace the solid quartz waveguide of Abela with the hollow waveguide of Brauer, because the hollow waveguide offers greater flexibility

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(Brauer, Abstract; col. 5, line 11; col. 7, lines 1-6) than a solid waveguide (Harrington, col. 1, lines 29-32 and 47-51), in particular because it was an art-recognized goal to introduce the laser into a living body to gain access in vivo to internal cells and tissues as discussed by Brauer, (col. 5, lines 10-18; claim 1).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Note: After January 13, 2004, the Examiner may be reached at (571) 272-0725, and should the Examiner be unavailable, inquiries may be directed to Deborah Reynolds, SPE of Art Unit 1632 at (571) 272-0734.

PETER PARAS  
PATENT EXAMINER



Valarie Bertoglio  
Examiner  
Art Unit 1632